



### REMARKS

The above-identified patent application has been reviewed in light of the Examiner's Action mailed 21 January 2003 (Paper No. 11). The status of the Claims is as follows: Claims 108-111, 113, 116, 122-142 and 145 were pending. Claim 135 has been cancelled without intending to abandon or to dedicate to the public any patentable subject matter. Claims 122 have been amended herein. Accordingly, following entry of the foregoing amendments, Claims 108-111, 113, 116, 122-134, 136-142 and 145 will be pending.

As set forth more fully below, reconsideration and withdrawal of the Examiner's rejections of the claims are respectfully requested.

#### Rejection to Improper Markush Group:

The Examiner has maintained the rejection of Claims 108-111, 122-134, 136-141, and extended the rejection to include Claim 113, as being drawn to an improper Markush group. Applicants have canceled Claim 135 and have amended Claim 122 to remove subject matter that is not within the Markush group.

#### Rejections Under 35 U.S.C. § 112, First and Second Paragraphs

The Examiner has maintained the rejection of Claims 122-134 and 136-142 under 35 U.S.C. § 112, first and second paragraphs, as being indefinite with respect to the definition of the linker group L. Applicants have amended Claim 122 to more narrowly recite the claimed linker group L within the Examiner's restriction group I and cancelled Claim 141. Claim 142 has been amended to depend from Claim 122. Thus, the pending claims, as amended, are sufficiently definite to meet the requirements of 35 U.S.C. § 112.

Claim Rejections Under 35 U.S.C. § 102

The Examiner has rejected Claims 108-111 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,521,160 (Chucholowski). The Examiner alleges that Chucholowski anticipates the claimed invention by teaching carboxystilbenes in Column 14, Examples 2 and 3.

Applicant respectfully submits that Chucholowski does not teach the presently claimed compounds.

As is evident from Examples 2 and 3 in Chucholowski, the carboxystilbenes only form a part of the final compounds taught. The final compounds taught are sulphuric acid esters of sugar alcohols, useful for treating atherosclerosis, not for modulating Fc Receptor binding. The Examiner's attention is directed to column 6, lines 41-45 of Chucholowski. From lines 41-42 it is clear that the carboxystilbenes referred to by the Examiner and described in Examples 2 and 3 are residues of formula (a). Residues of formula (a) are described earlier at column 2 lines 42-44. Such residues are examples of systems of conjugated double bonds that represent "B", a part of a final compound of formula (I). Compounds of formula (I) are the actual compounds of the invention described in Chucholowski. See column 1, line 42, and column 2, line 37, particularly column 2 lines 1-5, line 19 and line 37.

Thus, Chucholowski does not teach the compounds of the present invention *per se*, and their usefulness in inhibiting the Fc receptor. Chucholowski merely describes the incorporation of dicarboxylic acids having formula (a) (see below columns 1 and 2) in final products that are sulphuric acid esters of sugar alcohols and that have a formula represented by (I) as shown in column 2. Applicants therefore submit that Chucholowski does not anticipate the instant claims and respectfully request the Examiner's rejection under 35 U.S.C. § 102(b) be withdrawn.

Claim Rejections Under 35 U.S.C. § 103

The Examiner has rejected Claims 108-111, 113 and 116 under 35 U.S.C. § 103(a) over U.S. Patent No. 5,932,575 (Yanaka). The Examiner states that the present claims differ from Yanaka only with respect to the position of the carboxyl group in R<sup>5</sup>. The Examiner further states that one skilled in the art of formulation chemistry would have been motivated to prepare a composition of the present claims having a carboxyl group in the appropriate position to treat cardiac disease.

Applicants note that the subject matter as a whole is distinct from that to which Yanaka pertains. Firstly, it is clear that Yanaka relates to agents for treating cardiac diseases, and which act via the angiotensin receptors. Importantly, the compounds were designed so that they affected only one type of the angiotensin receptor, the AT2 receptor. See the Abstract and Example 2 at column 18. Thus, the compound referred to by the Examiner differs from those of the present invention, in respect of the rationale underlying the design and the desired function. Yanaka pertains to cardiac diseases, not immune diseases. Therefore, there is no motivation for one of skill in the art of immune diseases to modify or synthesize isomers of chemicals reported to have activity in the inhibition of the AT2 receptor to arrive at isomers of chemicals that will have activity in binding to Fc receptors.

As described in the instant specification, the compounds of the present invention were designed using knowledge of the structure of the Fc receptor, and its putative binding site with an antibody Fc region. See page 9, line 7 through page 13, line 4 of the specification. These compounds were designed so that the aromatic residues form hydrophobic interactions with two phenylalanines, and electrostatic interactions with two lysine residues, in the groove of the dimeric Fc receptor. This groove is believed to be the antibody Fc – Fc receptor interface regions. The structure of the linker between the two aromatic residues in a compound of the invention is such that

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it is able to span the distance between the two aromatic rings, while allowing for effective interaction between the compound and the relevant residues in the groove of the receptor. Thus, there would have been no motivation nor would it have been obvious to synthesize the compounds of the present invention that fulfill the binding characteristics described above by modifying angiotensin AT2 receptor blockers. Further, it would also be evident to a skilled artisan that the compounds of the present invention entail routes of design and production that differ from that to be taken if the compound cited by the Examiner was to be produced.

*intended use*

Applicants also note that Yanaka in no way describes actual production of the compounds of the present invention. See Table 1 in the column headed "R<sup>12</sup>." It is evident that in all 14 compounds made, R<sup>11</sup> was an N-derivative only. Thus, Yanaka does not enable the production of the compounds that the Examiner argues render obvious the compounds of the present invention. For these reasons, Applicants submit that Yanaka does not render obvious the compounds of the present invention and request that the Examiner's rejection under 35 U.S.C. § 103(a) be withdrawn.

Based upon the foregoing, Applicants believe that all pending claims are in condition for allowance and such disposition is respectfully requested. In the event that a telephone conversation would further prosecution and/or expedite allowance, the Examiner is invited to contact the undersigned.

Respectfully submitted,

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